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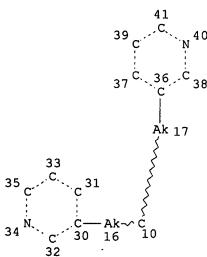
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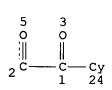
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STEREO ATTRIBUTES: NONE

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L22

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L17 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN

AN 1998:157415 CAPLUS

DN 128:205136

TI Preparation of acylated amino acid derivatives for multi-drug resistance therapies and immune suppression.

IN Armistead, David M.; Harding, Matthew W.; Saunders, Jeffrey O.; Boger, Joshua S.

PA Vertex Pharmaceuticals Inc., USA

SO U.S., 34 pp., Cont.-in-part of U.S. 5,620,971.

CODEN: USXXAM

DT Patent

LA English

FAN.CNT 4

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ΡI	US 5723459	Α	19980303	US 1995-377315	19950124
	US 5620971	A	19970415	US 1994-217982	19940325
PRAI	US 1991-697785	B2	19910509		
	US 1992-881152	B2	19920511		
	US 1992-952299	B2	19920928		
	US 1993-127814	B2	19930928		
	US 1994-217982	A2	19940325		
os	MARPAT 128:205136			·	
CT					

Ι

AB The present invention relates to novel acylated amino acid esters I [A = CH2, O, NH, alkylimino; B, D = (un)substituted (hetero)aryl, alk(en)(yn)yl, cycloalk(en)ylalk(en)(yn)yl, (hetero)aralkyl, cis-C(Q):CHT; Q = H, alk(en)(yn)yl; T = (un)substituted (hetero)aryl, substituted cycloalkyl; L = H, U; M = O, CHU; U = H, alk(en)yl, cycloalk(en)ylalk(en)yl, (hetero)aralk(en)yl, (hetero)aryl; J = H, alkyl, CH2Ph; K = alkyl, CH2Ph, cyclohexylmethyl; or JK = atoms to form 5- to 7-membered, optionally O- or S-containing heterocycle; m = 0-3; various provisos], as well as pharmaceutical compns. comprising them, which possess a broad range of useful biol. activities. These compds. can maintain, increase, or restore sensitivity of cells to therapeutic or prophylactic agents. They can also suppress, modify, or significantly

III

reduce an immune response, including an autoimmune response in a mammal. This invention also relates to pharmaceutical compns. comprising these compds. The compds. and pharmaceutical compns. of this invention are particularly well-suited for treatment of multi-drug resistant cells, for prevention of the development of multi-drug resistance, for use in multi-drug resistant cancer therapy, and for prevention or treatment of graft rejection and various autoimmune diseases. Over 100 I are reported, including both single and mixed diastereomers. Thus, 3-PhOC6H4CH2OH underwent oxidation to the aldehyde and reaction with Ph(CH2)3MgBr to give the racemic alc. 3-PhOC6H4CH(OH)(CH2)3Ph (II). Esterification of II with (S)-N-[(3,4,5-trimethoxyphenyl)glyoxyl]pipecolic acid (preparation given) yielded ester III as a mixture of diastereomers. In a test for reversal of multi-drug-resistance by a line of L1210 cells, selected I gave up to 18-fold in crease in the antiproliferative potency of doxorubicin.

IT 159997-95-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of acylated amino acid esters for multi-drug resistance therapies and immune suppression.)

RN 159997-95-2 CAPLUS

CN L-Proline, 1-[oxo(3,4,5-trimethoxyphenyl)acetyl]-, 4-(3-pyridinyl)-1-[3-(3-pyridinyl)propyl]butyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

$$(CH_2)_3$$
 O OMe OMe

RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN

AN 1997:307496 CAPLUS

DN 126:272378

TI Methods and compositions for stimulating neurite growth using compounds with affinity for FKBP12 in combination with neurotrophic factors

IN Armistead, David M.

PA Vertex Pharmaceuticals Incorporated, USA

SO S. African, 54 pp. CODEN: SFXXAB

DT Patent

LA English

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                           Α3
                                 19970228
     MARPAT 126:272378
OS
AB
     A pharmaceutically acceptable composition is disclosed which comprises (a) a
     FKBP12 e.g. having the formula BAC(:0)CH(K)N(J)C(:0)C(:E)D [A = 0, NH,
     cycloalkyl, etc.; D = U; E = O, CHU (if D = H, then E = CH-U; if E = O,
     then D is not H); U = H, O-(C1-4)-straight or branched alkyl,
     O-(C2-4)-straight or branched alkenyl, C1-6 (branched) alkyl, C2-6
```

AB A pharmaceutically acceptable composition is disclosed which comprises (a) neurotrophic amount of a compound with affinity for FK-506-binding protein FKBP12 e.g. having the formula BAC(:0)CH(K)N(J)C(:0)C(:E)D [A = 0, NH, N(C1-4 alkyl); B = H, C1-6 (branched) alkyl, C2-6 (branched) alkenyl, C5-7 cycloalkyl, etc.; D = U; E = 0, CHU (if D = H, then E = CH-U; if E = 0, then D is not H); U = H, O-(C1-4)-straight or branched alkyl, O-(C2-4)-straight or branched alkenyl, C1-6 (branched) alkyl, C2-6 (branched) alkenyl, (substituted) C5-7 cycloalkenyl, etc.; J = H, C1-2 alkyl; K = C1-4 (branched) alkyl, benzyl, cyclohexylmethyl, or J and K taken together form 5-7 membered heterocyclic ring which may contain O, S, SO, SO2; and the stereochem. at carbon to which K is bonded = R or S] and pharmaceutically acceptable derivs. thereof; (b) a neurotrophic factor; and (c) a pharmaceutically carrier. The neurotrophic factor may be e.g. nerve growth factor. The methodol. of the invention can be used to promote repair of neuronal damage caused by disease or phys. trauma.

IT 159997-95-2

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(compds. with affinity for FKBP12 in combination with neurotrophic factors for stimulating neurite growth)

RN 159997-95-2 CAPLUS

CN L-Proline, 1-[oxo(3,4,5-trimethoxyphenyl)acetyl]-, 4-(3-pyridinyl)-1-[3-(3-pyridinyl)propyl]butyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

$$(CH_2)_3$$
 O $(CH_2)_3$ O $(CH$

L17 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN

AN 1997:276774 CAPLUS

DN 126:343875

TI Preparation of acylated amino acid derivatives for multi-drug resistance therapies and immune suppression.

IN Armistead, David M.; Saunders, Jeffrey O.; Boger, Joshua S.

PA Vertex Pharmaceuticals Incorporated, USA

SO U.S., 35 pp., Cont.-in-part of U.S. Ser. No. 881,152, abandoned. CODEN: USXXAM

DT Patent

LA English

FAN.CNT 4

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PI	US 5620971	Α	19970415	US 1994-217982	19940325
	US 5723459	Α	19980303	US 1995-377315	19950124
PRAI	US 1991-697785	B2	19910509		
	US 1992-881152	B2	19920511		
	US 1992-952299	B2	19920928		
	US 1993-127814	B2	19930928		
	US 1994-217982	A2	19940325		
os	MARPAT 126:343875				
GT					

$$\begin{array}{c|c}
X & B \\
M & O \\
L
\end{array}$$

I

III

AB The present invention relates to novel acylated amino acid esters I [A = CH2, O, NH, alkylimino; B, D = (un)substituted (hetero)aryl,

alk(en)(yn)yl, cycloalk(en)ylalk(en)(yn)yl, (hetero)aralkyl, cis-C(Q):CHT; Q = H, alk(en)(yn)yl; T = (un)substituted (hetero)aryl, substitutedcycloalkyl; L = H, U; M = O, CHU; U = H, alk(en)yl, cycloalk(en)ylalk(en)yl, (hetero)aralk(en)yl, (hetero)aryl; J = H, alkyl, CH2Ph; K = alkyl, CH2Ph, cyclohexylmethyl; or JK = atoms to form 5- to 7-membered, optionally 0- or S-containing heterocycle; m = 0-3; various provisos], as well as pharmaceutical compns. comprising them, which possess a broad range of useful biol. activities. These compds. can maintain, increase, or restore sensitivity of cells to therapeutic or prophylactic agents. They can also suppress, modify, or significantly reduce an immune response, including an autoimmune response in a mammal. This invention also relates to pharmaceutical compns. comprising these compds. The compds. and pharmaceutical compns. of this invention are particularly well-suited for treatment of multi-drug resistant cells, for prevention of the development of multi-drug resistance, for use in multi-drug resistant cancer therapy, and for prevention or treatment of graft rejection and various autoimmune diseases. Over 100 I are reported, including both single and mixed diastereomers. Thus, 3-PhOC6H4CH2OH underwent oxidation to the aldehyde and reaction with Ph(CH2)3MgBr to give the racemic alc. 3-PhOC6H4CH(OH)(CH2)3Ph (II). Esterification of II with (S)-N-[(3,4,5-trimethoxyphenyl)glyoxyl]pipecolic acid (preparation given) yielded ester III as a mixture of diastereomers. In a test for reversal of multi-drug-resistance by a line of L1210 cells, selected I gave up to 18-fold increase in the antiproliferative potency of doxorubicin.

·IT 159997-95-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of acylated amino acid esters for multi-drug resistance therapies and immune suppression.)

RN 159997-95-2 CAPLUS

CN L-Proline, 1-[oxo(3,4,5-trimethoxyphenyl)acetyl]-, 4-(3-pyridinyl)-1-[3-(3-pyridinyl)propyl]butyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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L17
     ANSWER 4 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN
AN
     1995:274880 CAPLUS
DN
     122:55896
     1-(2-oxoacetyl)piperidine-2-carboxylic acid derivatives as
TI
     multi-drug-resistant cancer cell sensitizers
IN
     Armistead, David M.; Saunders, Jeffrey O.; Boger, Joshua S.
PA
     Vertex Pharmaceuticals Inc., USA
SO
     PCT Int. Appl., 111 pp.
     CODEN: PIXXD2
DT
     Patent
LA
     English
FAN.CNT 4
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os	MAI	TAGS	122:	5589	6.													
GI																		

AB The invention relates to compds. I [A = CH2, O, NH, alkylimino; B, D = (un)substituted (hetero)aryl, alk(en)(yn)yl, cycloalk(en)ylalk(en)(yn)yl, (hetero)aralkyl, cis-C(Q):CHT; Q = H, alk(en)(yn)yl; T = (un)substituted (hetero)aryl, substituted cycloalkyl; L = H, U; M = O, CHU; U = H, alk(en)yl, cycloalk(en)ylalk(en)yl, (hetero)aralk(en)yl, (hetero)aryl; J = H, alkyl, CH2Ph; K = alkyl, CH2Ph, cyclohexylmethyl; or JK = atoms to form 5- to 7-membered, optionally O- or S-containing heterocycle; m = 0-3; various provisos], as well as pharmaceutical compns. comprising them. The compds. maintain, increase, or restore sensitivity of cells to therapeutic or prophylactic agents, and are particularly well-suited for treatment or prevention of multi-drug resistant cancer cells. Over 100 I are reported, including both single and mixed diastereomers. For example,

3-PhOC6H4CH2OH underwent oxidation to the aldehyde and reaction with Ph(CH2)3MgBr to give the racemic alc. 3-PhOC6H4CH(OH)(CH2)3Ph. Esterification of this with (S)-N-[(3,4,5-trimethoxyphenyl)glyoxyl]pipecol ic acid (preparation given) yielded the ester II as a mixture of diastereomers. In a test for reversal of multi-drug-resistance by a line of L1210 cells, selected I gave up to 18-fold increase in the antiproliferative potency of doxorubicin.

IT 159997-95-2P

RL: SPN (Synthetic preparation); PREP (Preparation) (preparation of, as sensitizer for multi-drug-resistant cancer cells)

RN 159997-95-2 CAPLUS

CN L-Proline, 1-[oxo(3,4,5-trimethoxyphenyl)acetyl]-, 4-(3-pyridinyl)-1-[3-(3-pyridinyl)propyl]butyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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ANSWER 16 OF 16 CAPLUS COPYRIGHT 2007 ACS on STN
L23
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     1997:400101 CAPLUS
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     127:23742
     Method, compositions and kits for increasing the oral bioavailability of
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     pharmaceutical agents
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PA
     Baker Norton Pharmaceuticals, Inc., USA
SO
     PCT Int. Appl., 136 pp.
     CODEN: PIXXD2
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                                            NO 1997-2968
                                                                   19970625
     NO 321091
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     HK 1001960
                         A1
                                20060127
                                            HK 1998-101042
                                                                   19980211
     AU 200235584
                        Α
                                20020606
                                            AU 2002-35584
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     AU 784159
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                                20060216
PRAI US 1995-7071P
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                                19951026
     US 1996-608776
                         Α
                                19960229
     US 1996-733142
                          Α
                                19961016
     WO 1996-IB1485
                          W
                                19961024
     AU 1998-71300
                                19980422
                          A3
AB
     A method of increasing the bioavailability upon oral administration of a
     pharmacol. active target agent, particularly an antitumor or
     antineoplastic agent which exhibits poor or inconsistent oral
     bioavailability (e.g., paclitaxel, docetaxel or etoposide), comprises the
     oral co-administration to a mammalian patient of the target agent and an
     oral bioavailability-enhancing agent (e.g., cyclosporin A, cyclosporin D,
     cyclosporin F, or ketoconazole). The oral bioavailability-enhancing
     agents are known to be MDR (P-glycoprotein) inhibitors. The enhancing
     agent may be administered orally from 0.5-24 h prior to the oral
     administration of one or more doses of the target agent, substantially
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simultaneously with the target agent, or both prior to and substantially

simultaneously with the target agent. A method of treating mammalian patients suffering from diseases responsive to target agents with poor oral bioavailability, as well as oral dosage forms containing such target agents, combination oral dosage forms containing bioavailability-enhancing agents and target agents kits containing enhancing and target agent dosage forms and dosing information for the co-administration of the same are also disclosed.

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=> d bib abs 1-15
     ANSWER 1 OF 16 CAPLUS COPYRIGHT 2007 ACS on STN
     2007:86292 CAPLUS
AN
DN
     146:169222
ΤI
     Compositions of placentally-derived stem cells for the treatment of cancer
IN
     Ichim, Thomas E.
PΑ
     Medistem Laboratories, Inc., USA
SO
     PCT Int. Appl., 41pp.
     CODEN: PIXXD2
DT
     Patent
LA
     English
FAN.CNT 1
     PATENT NO.
                        KIND
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     WO 2007011693
                        A2 20070125 WO 2006-US27305 20060712
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         RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
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             GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM
     US 2007041954
                         A1
                                20070222
                                         US 2006-486635
                                                                   20060713
PRAI US 2005-699579P
                         Р
                                20050714
     Disclosed are prepns. of placentally-derived stem cells and compns. useful
     for the treatment of cancer. Said stem cells and compns. function through
     inducing a "guided differentiation" program in cancer cells, thereby
     reducing malignancy. Further extension of the invention pertains to
     augmenting ability of administered cells to induce differentiation through
     the co-administration of known differentiation inducing agents. Within
     the context of this disclosure, methods for inducing host responses to
     cancer are also described.
    ANSWER 2 OF 16 CAPLUS COPYRIGHT 2007 ACS on STN
     2006:1099544 CAPLUS
AN
DN
     145:432182
ΤI
     Method for treating prostate conditions
IN
     Smith, Gary J.; Huss, Wendy J.
PA
     U.S. Pat. Appl. Publ., 20pp.
SO
     CODEN: USXXCO
DT
     Patent
LΑ
    English
FAN.CNT 1
                        KIND DATE
     PATENT NO.
                                          APPLICATION NO.
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20061019 US 2006-350171

20060208

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US 2006233809

A1

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WO 2007037782
                                20070405
                          A2
                                             WO 2006-US4523
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             CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
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             KG, KZ, MD, RU, TJ, TM
PRAI US 2005-651101P
                          Ρ
                                20050208
     The invention provides a method for inhibiting the aberrant growth of
     cells in a prostate tissue in an individual comprising administering to
     the individual an amount of an inhibitor of the Breast Cancer Resistance
     Protein (BCRP/ABCG2), where the amount of the BCRP inhibitor is effective to
     inhibit the growth of the aberrantly growing cells. The method is also
     useful for treating prostate tumors or benign prostatic
     hyperplasia/hypertrophy (BPH). Also disclosed is the phenotype for
     prostate stem cells as determined by immunohistochem. localization methods.
     The prostate stem cells are pos. for BCRP protein, neg. for androgen
     receptor protein, neg. for p63 protein, and neg. for synaptophysin.
     ANSWER 3 OF 16 CAPLUS COPYRIGHT 2007 ACS on STN
     2006:566785 CAPLUS
     145:55958
     Method for treatment and prevention of epilepsy
     Nedergaard, Maiken; Tian, Guo Feng
     University of Rochester, USA
     PCT Int. Appl., 122 pp.
     CODEN: PIXXD2
     Patent
     English
FAN.CNT 1
     PATENT NO.
                         KIND
                                DATE
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                                          WO 2005-US41058
     WO 2006062683
                         A2
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             VN, YU, ZA, ZM, ZW
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             CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
             GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM
PRAI US 2004-627847P
                         P
                                20041115
     The invention is directed to a method of treating or preventing epileptic
     seizures in a subject and a method of inhibiting hypersynchronous burst
     activity of neurons by administering an agent which interferes with
     glutamate, aspartate, and/or ATP release from astrocytes. Also presented
     is a method of identifying agents suitable for treating or preventing
     epileptic seizures.
    ANSWER 4 OF 16 CAPLUS COPYRIGHT 2007 ACS on STN
     2005:426232 CAPLUS
     142:477356
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IN
     Li, Shengwen; Aoki, Kei Roger
     Allergan, Inc., USA
U.S. Pat. Appl. Publ., 61 pp.
PA
SO
     CODEN: USXXCO
DT
     Patent
LA
     English
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                                            APPLICATION NO.
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PΙ
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                                             US 2003-715810
                                                                     20031117
     US 7172764
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     AU 2004291152
                          A1
                                 20050602
                                             AU 2004-291152
                                                                     20041115
     CA 2546383
                                 20050602
                          A1
                                             CA 2004-2546383
                                                                     20041115
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                                 20050602
                                             WO 2004-US38320
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             NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
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     EP 1684799
                          A2
                                 20060802
                                             EP 2004-816954
                                                                     20041115
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             HR, IS, YU
PRAI US 2003-715810
                                 20031117
                          Α
     WO 2004-US38320
                          W
                                 20041115
     The present invention relates to rescue agents for use in the treatments
AB
     of toxin intoxication-for example botulinum intoxication, which can result
     from food poisoning, an act of bioterrorism, or from accidental overdose
     in the course of treatment. In some embodiments, the rescue agents
     comprise at least one of an inactive botulinum toxin and a modified
     nontoxic nonhemagglutinin. The present invention also provides for
     glycosylated active and inactive toxins and methods of using same.
              THERE ARE 109 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE.CNT 109
              ALL CITATIONS AVAILABLE IN THE RE FORMAT
L23
     ANSWER 5 OF 16 CAPLUS COPYRIGHT 2007 ACS on STN
ΑN
     2005:216616 CAPLUS
DN
     142:285198
     Ultrasonic concentration of drug delivery capsules
TI
     Dayton, Paul; Ferrara, Katherine W.; Shortencarier, Michaelann; Bloch,
IN
PA
     The Regents of the University of California, USA
SO
     PCT Int. Appl., 67 pp.
     CODEN: PIXXD2
DT
     Patent
LΑ
     English
FAN.CNT 1
     PATENT NO.
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PΙ
     WO 2005020918
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                         A2
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                                                                    20040827
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             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
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Rescue agents for treating botulinum toxin intoxications

ΤI

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NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
             TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
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             SN, TD, TG
     US 2005084538
                                 20050421
                                             US 2004-928648
                                                                     20040826
     EP 1663109
                                 20060607
                           A2
                                             EP 2004-782415
                                                                     20040827
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PRAI US 2003-498405P
                                 20030827
                          P
     US 2004-928648
                          Α
                                 20040826
     WO 2004-US27931
                          W
                                 20040827
     Methods, compns. and apparatus for localized delivery of compds. are provided.
AB
     In certain embodiments, radiation force is used to direct carriers to a
     target site, and addnl. radiation is used to fragment the localized
     carriers, releasing associate compds. Ultrasound radiation is preferred as
     the source for radiation force and for fragmentation. Also encompassed
     are embodiments in which targeting and fragmentation are combined with
     imaging of the treatment site. Alternate embodiments are disclosed in
     which compds. are locally delivered without use of carriers.
     Acoustically-active lipospheres (AALs) containing Sudan Black dye were
     produced. Mice were injected with AALs containing Sudan Black showed that
     there was increased deposition of the dye in the region of tissue
     subjected to insonation. AALs containing Sudan Black were also shown to
     adhere to endothelial cells.
     ANSWER 6 OF 16 CAPLUS COPYRIGHT 2007 ACS on STN
L23
AN
     2005:136528 CAPLUS
     142:212405
DN
TI
     Means and methods for treating a disease which is associated with an
     excess transport of hyaluronan across a lipid bilayer
ΙN
     Prehm, Peter
PA
     Universitaetsklinikum Muenster, Germany
so
     PCT Int. Appl., 200 pp.
     CODEN: PIXXD2
DT
     Patent
LA
     English
FAN.CNT 1
     PATENT NO.
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     WO 2005013947
PΙ
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     WO 2005013947
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             NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
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             SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
             SN, TD, TG
     AU 2004262494 -
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                                             AU 2004-262494
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     CA 2533846
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                                             CA 2004-2533846
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     EP 1660072
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                                20060531
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PRAI EP 2003-16615
                        Α
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     EP 2003-17374
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EP 2003-25102
                    Α
                          20031031
EP 2004-12369
                    Α
                          20040525
WO 2004-EP8547
                   W
                          20040729
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AB The present invention relates to the use of at least one inhibitor of at least one ABC-transporter capable of transporting hyaluronan across a lipid bilayer, for the preparation of a pharmaceutical composition for the treatment

of a disease which is associated with an excess transport of hyaluronan across a lipid bilayer, e.g. arthritis. Furthermore, the present invention relates to a method for screening a compound which is suitable for the treatment of a disease which is associated with an excess transport of hyaluronan across a lipid bilayer, e.g. arthritis. The present invention also relates to a method for screening a compound which reduces the transport of hyaluronan mediated by (an) ABC-transporter(s). Furthermore, the present invention relates to a method for identifying a subject at risk for a disease which is associated with an excess transport of hyaluronan across a lipid bilayer, e.g. arthritis as well as to a method of screening for a compound which is suitable for the treatment of a disease which is associated with an excess transport of hyaluronan across a lipid bilayer, e.g. arthritis in a subject. In addition, the present invention relates to a method of preventing, ameliorating and/or treating the symptoms of a disease which is associated with an excess transport of hyaluronan across a lipid bilayer, e.g. arthritis in a subject.

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L23
    ANSWER 7 OF 16 CAPLUS COPYRIGHT 2007 ACS on STN
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AN 2005:76266 CAPLUS

DN 142:148758

Augmenting the activity of antibacterial agents using efflux pump ΤI

IN Grossman, Trudy Hope

PA Vertex Pharmaceuticals Incorporated, USA

SO PCT Int. Appl., 139 pp. CODEN: PIXXD2

DΤ Patent

LA English

FAN.CNT 1

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PATENT NO.
                       KIND
                              DATE APPLICATION NO.
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                       A1 20050127 WO 2004-US21973 20040709
PΙ
    WO 2005007162
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            NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
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    US 2005090482
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PRAI US 2003-486041P
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    US 2003-486046P
                        P
                              20030710
    US 2003-486102P
                        Ρ
                              20030710
    US 2003-486235P
                        Ρ
                              20030710
OS
    MARPAT 142:148758
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AB The present invention relates to compds. that potentiate the activity of antibacterials. The present invention also relates to compns. useful in treating bacterial infection in mammals, and methods therewith. The present invention also relates to a method of inhibiting bacterial efflux of an antibiotic, thereby increasing the efficacy of the antibiotic. THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

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ANSWER 8 OF 16 CAPLUS COPYRIGHT 2007 ACS on STN
ΑN
     2004:1036851 CAPLUS
DN
     142:696
TI
     Synergistic treatment of cancer using immunomers in conjunction with
     chemotherapeutic agents
IN
     Kandimalla, Ekambar R.; Agrawal, Sudhir; Wang, Dagin
PA
     Hybridon, Inc., USA
SO
     PCT Int. Appl., 106 pp.
     CODEN: PIXXD2
DT
     Patent
LΑ
     English
FAN.CNT 1
     PATENT NO.
                          KIND
                                 DATE
                                             APPLICATION NO.
                                                                      DATE
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PΙ
     WO 2004103301
                           A2
                                  20041202
                                              WO 2004-US15313
                                                                      20040514
     WO 2004103301
                           Α3
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             AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
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             NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
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              SN, TD, TG
     AU 2004241093
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     EP 1628531
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                                              EP 2004-752345
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     JP 2006528697
                           Т
                                 20061221
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PRAI US 2003-471247P
                           Ρ
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     WO 2004-US15313
                          W
                                 20040514
os
     MARPAT 142:696
     The invention discloses the therapeutic use of immunostimulatory
AB
     oligonucleotides and/or immunomers in combination with chemotherapeutic
     agents to provide a synergistic therapeutic effect.
L23
     ANSWER 9 OF 16 CAPLUS COPYRIGHT 2007 ACS on STN
AN
     2003:202416 CAPLUS
     138:226752
DN
     Vaginal delivery of drugs and inhibitors of membrane efflux systems for
TI
     cancer therapy
     Pauletti, Giovanni M.; Liu, James H.; Benet, Leslie Z.; Ritschel, Wolfgang
IN
PA
     UMD, Inc., USA
     PCT Int. Appl., 61 pp.
SO
     CODEN: PIXXD2
DT
     Patent
LΑ
     English
FAN.CNT 12
     PATENT NO.
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                                 DATE
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PΙ
     WO 2003020210
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                                                                     20020821
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     JP 2005507874
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PRAI US 2001-315877P
                           Ρ
                                 20010829
     AU 1998-76976
                           А3
                                 19980610
     WO 2002-US27027
                           W
                                 20020821
AΒ
     Devices, methods, and compns. for cancer therapy by administration of
     chemotherapeutic agents and/or inhibitors of membrane efflux systems to
     the vagina for topical and systemic tumor targets are disclosed. Vaginal
     suppositories were prepared from verapamil-HCl 0.75, HPMC 600, and
     Transcutol 600 mg, Suppocire AS2 4.8 (for 8 suppositories).
L23
     ANSWER 10 OF 16 CAPLUS COPYRIGHT 2007 ACS on STN
AN
     2002:241334 CAPLUS
DN
     136:257275
TI
     Method and composition for modulating amyloidosis
IN
     Reiner, Peter B.; Lam, Fred Chiu-Lai
PA
SO
     U.S. Pat. Appl. Publ., 38 pp., Cont.-in-part of U.S. Ser. No. 67,523,
     abandoned.
     CODEN: USXXCO
DT
     Patent
LА
     English
FAN.CNT 3
     PATENT NO.
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                                 DATE
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                                                                     DATE
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PΙ
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     US 2002037843
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                                 20020328
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PRAI US 1997-847616
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     US 1998-177413
                          Α
                                 19981023
     WO 1999-US23885
                          W
                                 19991014
AB
     Methods for modulating amyloid deposition in a subject are described. An
```

effective amount of at least one ATP binding cassette (ABC) transporter

blocker is administered to a subject, such that modulation of amyloid deposition occurs. Methods also include administering and effective amount of at least one ABC transporter blocker, or a pharmaceutically acceptable salt thereof, to a subject such that a disease state associated with amyloidosis is treated. Packaged pharmaceutical compns. for treating amyloidosis are described. The package includes a container for holding an effective amount of a pharmaceutical composition and instructions for using the pharmaceutical composition for treatment of amyloidosis. The pharmaceutical composition includes at least one ABC blocker for modulating amyloid deposition in a subject. Methods for identifying agents which modulate amyloid deposition in a subject are also described. An effective amount of at least one ATP binding cassette (ABC) transporter blocker is administered to an organism, such that modulation of amyloid deposition occurs.

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L23
     ANSWER 11 OF 16 CAPLUS COPYRIGHT 2007 ACS on STN
ΑN
     2001:935435 CAPLUS
DN
     136:84677
TI
     Methods for enhancing antibody-induced cell lysis and treating cancer
IN
     Weiner, George; Hartmann, Gunther
PA
     University of Iowa Research Foundation, USA
SO
     PCT Int. Appl., 312 pp.
     CODEN: PIXXD2
DT
     Patent
LA
     English
FAN.CNT 1
     PATENT NO.
                        KIND
                                DATE
                                           APPLICATION NO.
                                                                    DATE
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     WO 2001097843
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             BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
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     AU 2006216542
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PRAI US 2000-213346P
                         P
                                20000622
     AU 2001-270134
                         A3
                                20010622
     WO 2001-US20154
                         W
                                20010622
AB
     The invention relates to methods and products for treating cancer. In
     particular the invention relates to combinations of nucleic acids and
     antibodies for the treatment and prevention of cancer. The invention also
     relates to diagnostic methods for screening cancer cells.
L23
    ANSWER 12 OF 16 CAPLUS COPYRIGHT 2007 ACS on STN
AN
     2000:475560 CAPLUS
DN
     133:109949
     Pharmaceutical compositions for treatment of diseased tissues
ΤI
IN
     Lee, Clarence C.; Lee, Feng-Min
PA
     USA
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PCT Int. Appl., 26 pp.

SO

CODEN: PIXXD2

DT Patent LA English FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
ΡI	WO 2000040269	A2	20000713	WO 2000-US191	20000105
	WO 2000040269	A3	20001130		

W: AU, CA, CN, JP

RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

PRAI US 1999-114906P P 19990105

AB A method to treat diseased tissue is provided where a cytotoxic compound is administered to a patient in need of treatment in combination with an immunostimulant. Diseased cells and/or infectious microbes/viruses are killed by the cytotoxic compound in the presence of the immunostimulant. The cell components including cellular contents and cell membrane fragments are presented by the immunostimulant to the host animal as antigens to stimulate the immune responses toward other diseased cells of the same type(s), that either remain in the vicinity or reside in distant tissues or organs. The cytotoxic mol. and immunostimulant are preferably applied locally at high concns., either sequentially or, preferably, simultaneously. For example, the composition can be administered directly to a target cancer. The composition can be prepared in various forms, such as a paste, a time release molded solid shape, a solution, a mixture with emulsifier, etc. Alternatively, the cytotoxic mol. and immunostimulant are applied in sequence.

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L23 ANSWER 13 OF 16 CAPLUS COPYRIGHT 2007 ACS on STN
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AN 2000:290832 CAPLUS

DN 132:318003

TI Method and composition for modulating amyloidosis

IN Reiner, Peter B.; Lam, Fred Chiu-lai

PA The University of British Columbia, Can.

SO PCT Int. Appl., 86 pp.

CODEN: PIXXD2

DT Patent LA English

FAN. CNT 3

2744.		CENT	NO.			KIN		DATE				ICAT				D	ATE	
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		2002								1	US 1	998-	1774	13		19	9981	023
		6514																
	CA	2348	019			A1		2000	0504	(CA 1	999-	2348	019		19	9991	014
	ΕP	1123	090			A1		2001	0816	1	EP 1	999-	9548	94		19	9991	014
		R:							FR,	GB,	GR,	IT,	LI,	LU,	NL,	SE,	MC,	PT,
						LV,												
		2002							0903								9991	014
	AU	7625	93			B2				1	AU 2	000-:	1112	В		19	9991	014
PRAI		1998						1998:										
		1997																
	US	1998	-6752	23		B 2		19980	0428									

WO 1999-US23885 W 19991014

Methods for modulating amyloid deposition in a subject are described. An AB effective amount of at least one ATP-binding cassette (ABC) transporter blocker is administered to a subject, such that modulation of amyloid deposition occurs. Methods also include administering an effective amount of at least one ABC transporter blocker, or a pharmaceutically acceptable salt thereof, to a subject such that a disease state associated with amyloidosis is treated. Packaged pharmaceutical compns. for treating amyloidosis are described. The package includes a container for holding an effective amount of a pharmaceutical composition and instructions for using the pharmaceutical composition for treatment of amyloidosis. The pharmaceutical composition includes at least one ABC blocker for modulating amyloid deposition in a subject. Methods for identifying agents which modulate amyloid deposition in a subject are also described. An effective amount of at least one ATP binding cassette (ABC) transporter blocker is administered to an organism, such that modulation of amyloid deposition occurs.

RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L23 ANSWER 14 OF 16 CAPLUS COPYRIGHT 2007 ACS on STN
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AN 1999:795653 CAPLUS

DN 132:30816

TI Methods and compositions using P-glycoprotein inhibitors for increasing penetration of HIV protease inhibitors

IN Brouwer, Kenneth Russell; Polli, Joseph William

PA Glaxo Group Limited, UK

SO PCT Int. Appl., 22 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PA	CENT :	NO.			KIN		DATE APPLICATION NO.					NO.						
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			ΙE,				•												
PRAI	GB	1998	-121	89		Α		1998	0605										
	WO	1999	-EP3	827		W		1999	0603										

AB The invention relates to methods for increasing penetration of HIV protease-inhibiting compds. into tissues expressing P-glycoprotein. Central nervous system penetration of an HIV protease inhibitor, e.g. amprenavir, is increased with administration of a P-glycoprotein inhibitor, e.g. 9,10-dihydro-5-methoxy-9-oxo-N-[4-(2-(1,2,3,4-tetrahydro-6,7-dimethoxy-2-isoquinolinyl)ethyl)phenyl]-4-5 acridinecarboxamide (GF120918).

L23 ANSWER 15 OF 16 CAPLUS COPYRIGHT 2007 ACS on STN

AN 1998:719248 CAPLUS

DN 130:510

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TI Method and composition for modulating amyloidosis
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SO PCT Int. Appl., 67 pp.

CODEN: PIXXD2

DT Patent LA English

FAN.CNT 3

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PRAI		1997				A2		1997	0428									•	
	WO	1998	-US8	463	_	W		1998	0428										
			_				_												

Methods for modulating amyloid deposition in a subject are described. An AB effective amount of at least one ATP-binding cassette (ABC) transporter blocker is administered to a subject, such that modulation of amyloid deposition occurs. Methods also include administering an effective amount of at least one ABC transporter blocker, or a pharmaceutically acceptable salt thereof, to a subject such that a disease state associated with amyloidosis is treated. Packaged pharmaceutical compns. for treating amyloidosis are described. The package includes a container for holding an effective amount of a pharmaceutical composition and instructions for using the pharmaceutical composition for treatment of amyloidosis. The pharmaceutical composition includes at least one ABC blocker for modulating amyloid deposition in a subject. Methods for identifying agents which modulate amyloid deposition in a subject are also described. An effective amount of at least one ATP binding cassette (ABC) transporter blocker is administered to an organism, such that modulation of amyloid deposition occurs.

IN Reiner, Peter B.; Lam, Fred Chiu-lai

PA The University of British Columbia, Can.

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Items	File	
258	5:	Biosis Previews(R) 1926-2007/Apr W1
351	34:	SciSearch(R) Cited Ref Sci 1990-2007/Apr W2
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		EMCare_2007/Apr W2
17	65:	Inside Conferences_1993-2007/Apr 16
243	71:	ELSEVIER BIOBASE_1994-2007/Apr W3
		EMBASE_1974-2007\(\overline{7}\)Apr 12
7	98:	General Sci Abs_1984-2007/Apr
		NewsRx Weekly Reports_1995-2007/Apr W2
186		Pascal_1973-2007/Apr W2
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		ToxFile_1965-2007/Apr W2
		Cancerlit_1975-2002/Oct
7		Global Health_1983-2007/Mar
3		EMBASE Alert_2007/Apr 12
		FEDRIP_2007/Mar
2		New Scientist_1994-2007/Dec W1
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6	444:	New England Journal of Med1985-2007/Apr W1

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HELP NEWS 5 for information.
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  File 71:ELSEVIER BIOBASE 1994-2007/Apr W3
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DIALOG(R) File 399:CA SEARCH(R)
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134115864
               CA: 134(9)115864n
                                    PATENT
  Preparation of neurotrophic tetrahydroisoquinolinecarboxylates and
  tetrahydrothienopyridinecarboxylates
  INVENTOR(AUTHOR): Macielag, Mark; Sui, Zhihua; Walsh, Shawn; Zhao, Boyu
  LOCATION: USA
  ASSIGNEE: Ortho-McNeil Pharmaceutical, Inc.
  PATENT: PCT International; WO 200104090 A2 DATE: 20010118
  APPLICATION: WO 2000US16072 (20000612) *US PV143098 (19990709)
  PAGES: 69 pp. CODEN: PIXXD2 LANGUAGE: English
  PATENT CLASSIFICATIONS:
    CLASS: C07D-000/A
  DESIGNATED COUNTRIES: AE; AG; AL; AM; AT; AU; AZ; BA; BB; BG; BR; BY; CA;
CH; CN; CR; CU; CZ; DE; DK; DM; DZ; EE; ES; FI; GB; GD; GE; GH; GM; HR; HU;
ID; IL; IN; IS; JP; KE; KG; KP; KR; KZ; LC; LK; LR; LS; LT; LU; LV; MA; MD;
MG; MK; MN; MW; MX; MZ; NO; NZ; PL; PT; RO; RU; SD; SE; SG; SI; SK; SL; TJ;
TM; TR; TT; TZ; UA; UG; UZ; VN; YU; ZA; ZW; AM; AZ; BY; KG; KZ; MD; RU; TJ;
TM DESIGNATED REGIONAL: GH; GM; KE; LS; MW; MZ; SD; SL; SZ; TZ; UG; ZW; AT
; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE; BF;
BJ; CF; CG; CI; CM; GA; GN; GW; ML; MR; NE; SN; TD; TG
  SECTION:
    CA227017 Heterocyclic Compounds (One Hetero Atom)
    CA201XXX Pharmacology
  IDENTIFIERS: tetrahydroisoquinolinecarboxylate
    tetrahydrothienyopyridinecarboxylate prepn neurotrophic
  DESCRIPTORS:
Nervous system...
    amyotrophic lateral sclerosis, treatment; prepn. of neurotrophic
    tetrahydroisoquinoline carboxylates and
    tetrahydrothienopyridinecarboxylates
Nerve, disease...
    diabetic neuropathy, treatment; prepn. of neurotrophic
    tetrahydroisoquinoline carboxylates and
    tetrahydrothienopyridinecarboxylates
Spinal cord...
    injury, treatment; prepn. of neurotrophic tetrahydroisoquinoline
    carboxylates and tetrahydrothienopyridinecarboxylates
Nerve, disease...
    peripheral, injury, treatment; prepn. of neurotrophic
    tetrahydroisoquinoline carboxylates and
    tetrahydrothienopyridinecarboxylates
Antiparkinsonian agents... Anti-Alzheimer's agents... Neurotrophic factors
    prepn. of neurotrophic tetrahydroisoquinoline carboxylates and
    tetrahydrothienopyridinecarboxylates
Brain, disease...
    stroke, treatment; prepn. of neurotrophic tetrahydroisoquinoline
    carboxylates and tetrahydrothienopyridinecarboxylates
Brain, disease...
    trauma, treatment; prepn. of neurotrophic tetrahydroisoquinoline
    carboxylates and tetrahydrothienopyridinecarboxylates
Paralysis...
    treatment of Bell's palsy; prepn. of neurotrophic
    tetrahydroisoquinoline carboxylates and
    tetrahydrothienopyridinecarboxylates
Multiple sclerosis...
    treatment; prepn. of neurotrophic tetrahydroisoquinoline carboxylates
    and tetrahydrothienopyridinecarboxylates
  CAS REGISTRY NUMBERS:
78183-55-8P 93449-83-3P 178205-92-0P 320578-48-1P 320578-49-2P
    320578-50-5P 320578-52-7P 320578-53-8P 320578-58-3P 320578-59-4P
    320578-61-8P 320578-62-9P 320578-64-1P 320578-65-2P
                                                            320578-67-4P
    320578-68-5P 320578-70-9P 320578-71-0P 320578-72-1P 320578-75-4P
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prepn. of neurotrophic tetrahydroisoquinoline carboxylates and
    tetrahydrothienopyridinecarboxylates
320578-51-6P 320578-54-9P 320578-55-0P 320578-56-1P 320578-57-2P
    320578-60-7P
                 320578-63-0P 320578-66-3P 320578-69-6P 320578-73-2P
    320578-74-3P 320578-79-8P prepn. of neurotrophic
    tetrahydroisoquinoline carboxylates and
    tetrahydrothienopyridinecarboxylates
931-51-1 1124-63-6 1609-86-5 1939-99-7 2859-67-8 3685-48-1 4075-59-6
    5781-53-3 20017-67-8 28276-08-6 52244-70-9 74163-81-8 88755-16-2
    128502-56-7 starting material; prepn. of neurotrophic
    tetrahydroisoquinoline carboxylates and
    tetrahydrothienopyridinecarboxylates
 3/5/2
           (Item 2 from file: 399)
DIALOG(R) File 399:CA SEARCH(R)
(c) 2007 American Chemical Society. All rts. reserv.
               CA: 133(9)120320r
  133120320
                                    PATENT
  Preparation of furopyridines and related compounds with neurotrophic
  activity.
  INVENTOR(AUTHOR): Peters, Dan; Gronborg, Mette; Moller, Arne
 LOCATION: Den.
 ASSIGNEE: Neurosearch A/S
  PATENT: PCT International; WO 200043397 Al DATE: 20000727
  APPLICATION: WO 2000DK12 (20000113) *DK 9961 (19990119)
  PAGES: 33 pp. CODEN: PIXXD2 LANGUAGE: English
  PATENT CLASSIFICATIONS:
    CLASS: C07D-491/048A; A61K-031/4355B; A61P-025/00B
  DESIGNATED COUNTRIES: AE; AL; AM; AT; AU; AZ; BA; BB; BG; BR; BY; CA; CH;
CN; CR; CU; CZ; DE; DK; DM; EE; ES; FI; GB; GD; GE; GH; GM; HR; HU; ID; IL;
IN; IS; JP; KE; KG; KP; KR; KZ; LC; LK; LR; LS; LT; LU; LV; MA; MD; MG; MK;
MN; MW; MX; NO; NZ; PL; PT; RO; RU; SD; SE; SG; SI; SK; SL; TJ; TM; TR; TT;
TZ; UA; UG; US; UZ; VN; YU; ZA; ZW; AM; AZ; BY; KG; KZ; MD; RU; TJ; TM
  DESIGNATED REGIONAL: GH; GM; KE; LS; MW; SD; SL; SZ; TZ; UG; ZW; AT; BE;
CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE; BF; BJ; CF;
CG; CI; CM; GA; GN; GW; ML; MR; NE; SN; TD; TG
  SECTION:
    CA228002 Heterocyclic Compounds (More Than One Hetero Atom)
    CA201XXX Pharmacology
  IDENTIFIERS: furopyridine prepn neurotrophic agent, neurodegeneration
    treatment furopyridine, traumatic lesion nervous system treatment
    furopyridine
  DESCRIPTORS:
Nervous system...
    amyotrophic lateral sclerosis, treatment; prepn. of furopyridines and
    related compds. with neurotrophic activity
Nerve...
    degeneration, treatment; prepn. of furopyridines and related compds.
    with neurotrophic activity
Mental disorder...
    dementia, treatment; prepn. of furopyridines and related compds. with
    neurotrophic activity
Nervous system...
    Huntington's chorea, treatment; prepn. of furopyridines and related
    compds. with neurotrophic activity
Brain, disease...
    ischemia, treatment; prepn. of furopyridines and related compds. with
    neurotrophic activity
Nerve, disease...
    neuropathy, treatment; prepn. of furopyridines and related compds. with
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320578-76-5P 320578-77-6P 320578-7P 320578-80-1P intermediate;

neurotrophic activity Nerve... peripheral, treatment of traumatic lesion; prepn. of furopyridines and related compds. with neurotrophic activity Antiparkinsonian agents... Anti-Alzheimer's agents... prepn. of furopyridines and related compds. with neurotrophic activity Spinal cord... treatment of traumatic lesion; prepn. of furopyridines and related compds. with neurotrophic activity CAS REGISTRY NUMBERS: 9061-61-4 potentiators; prepn. of furopyridines and related compds. with neurotrophic activity 99-81-0 109-65-9 177-11-7 2227-64-7 23081-86-9P 122031-10-1P 285547-51-5P 285547-52-6P 285547-53-7P 285547-54-8P 285547-55-9P 285547-56-0P 285547-58-2P 285547-59-3P 285547-60-6P 285547-61-7P 285547-62-8P 285547-63-9P 285547-64-0P prepn. of furopyridines and related compds. with neurotrophic activity 3/5/3 (Item 3 from file: 399) DIALOG(R) File 399:CA SEARCH(R) (c) 2007 American Chemical Society. All rts. reserv. 129067706 CA: 129(6)67706k PATENT Preparation of 1-phenylalkyl-1,2,3,6-tetrahydropyridines for treating Alzheimer's disease INVENTOR(AUTHOR): Baroni, Marco; Cardamone, Rosanna; Fournier, Jacqueline ; Guzzi, Umberto LOCATION: Fr. ASSIGNEE: Sanofi; Baroni, Marco; Cardamone, Rosanna; Fournier, Jacqueline ; Guzzi, Umberto PATENT: PCT International; WO 9825903 Al DATE: 19980618 APPLICATION: WO 97FR2286 (19971212) *FR 9615335 (19961213) PAGES: 29 pp. CODEN: PIXXD2 LANGUAGE: French PATENT CLASSIFICATIONS: CLASS: C07D-211/70A; C07D-401/04B; A61K-031/445B DESIGNATED COUNTRIES: AL; AM; AT; AU; AZ; BA; BB; BG; BR; BY; CA; CH; CN; CU; CZ; DE; DK; EE; ES; FI; GB; GE; GH; GM; GW; HU; ID; IL; IS; JP; KE; KG; KP; KR; KZ; LC; LK; LR; LS; LT; LU; LV; MD; MG; MK; MN; MW; MX; NO; NZ; PL; PT; RO; RU; SD; SE; SG; SI; SK; SL; TJ; TM; TR; TT; UA; UG; US; UZ; VN; YU; ZW; AM; AZ; BY; KG; KZ; MD; RU; TJ; TM DESIGNATED REGIONAL: GH; GM; KE; LS ; MW; SD; SZ; UG; ZW; AT; BE; CH; DE; DK; ES; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE; BF; BJ; CF; CG; CI; CM; GA; GN; ML; MR; NE; SN; TD; TG SECTION: CA227016 Heterocyclic Compounds (One Hetero Atom) CA201XXX Pharmacology CA263XXX Pharmaceuticals IDENTIFIERS: phenylalkyltetrahydropyridine prepn neurotrophic neuroprotecting activity, Alzheimer treatment phenylalkyltetrahydropyridine deriv, tetrahydropyridine phenylalkyl prepn neurotrophic neuroprotecting activity DESCRIPTORS: Alzheimer's disease... 1-phenylalkyl-1,2,3,6-tetrahydropyridines with neurotrophic and neuroprotecting activity for treatment of CAS REGISTRY NUMBERS:

CAS REGISTRY NUMBERS:

135-01-3 392-83-6 598-21-0 643-79-8 1595-07-9P 2402-78-0 3612-20-2 3637-01-2 65040-68-8 103323-56-4P 188396-79-4P 188396-80-7P 188396-81-8P 208989-20-2P 208989-22-4P 208989-24-6P 208989-30-4P 208989-32-6P 208989-34-8P for prepn. of 1-phenylalkyl-1,2,3,6-tetrahydropyridine deriv.

208989-01-9P 208989-03-1P 208989-05-3P 208989-07-5P 208989-09-7P

208989-11-1P 208989-12-2P 208989-14-4P 208989-16-6P 208989-18-8P prepn. of 1-phenylalkyl-1,2,3,6-tetrahydropyridines for treating Alzheimer's disease

(Item 1 from file: 34) DIALOG(R) File 34: SciSearch(R) Cited Ref Sci (c) 2007 The Thomson Corp. All rts. reserv. Genuine Article#: 469WL Number of References: 206 Title: Metabotropic glutamate receptor subtypes as targets for neuroprotective drugs Author(s): Bruno V; Battaglia G; Copani A; D'Onofrio M; Di Iorio P; De Blasi A; Melchiorri D; Flor PJ; Nicoletti F (REPRINT) Corporate Source: Univ Roma La Sapienza, Dept Human Physiol & Pharmacol, Piazzale Aldo Moro 5/I-00185 Rome//Italy/ (REPRINT); Univ Roma La Sapienza, Dept Human Physiol & Pharmacol, I-00185 Rome//Italy/; INM Neuromed, Pozzilli//Italy/; Univ Catania, Dept Pharmaceut Sci, Catania // Italy /; Univ Chieti, Dept Biomed Sci, Chieti // Italy /; Novartis Pharma AG, Nervous Syst Res, Basel//Switzerland/ Journal: JOURNAL OF CEREBRAL BLOOD FLOW AND METABOLISM, 2001, V21, N9 (SEP)

ISSN: 0271-678X Publication date: 20010900

Publisher: LIPPINCOTT WILLIAMS & WILKINS, 530 WALNUT ST, PHILADELPHIA, PA 19106-3621 USA

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, P1013-1033

Journal Subject Category: ENDOCRINOLOGY & METABOLISM; HEMATOLOGY;

NEUROSCIENCES Abstract: Metabotropic glutamate (mGlu) receptors have been considered as potential targets for neuroprotective drugs. but the lack of specific drugs has limited the development of neuroprotective strategies in experimental models of acute or chronic central nervous system (CNS) disorders. The advent of potent and centrally available subtype-selective ligands has overcome this limitation, leading to an extensive investigation of the role of mGlu receptor subtypes in neurodegeneration during the last 2 years. Examples of these drugs are the noncompetitive mGlul receptor antagonists, CPCCOEt and BAY-36-7620; the noncompetitive mGlu5 receptor antagonists, 2-methyl-6-(phenylethynyl)pyridine, SIB-1893, and SIB-1757; and the potent mGlu2/3 receptor agonists, LY354740 and LY379268. Pharmacologic blockade of mGlu I or mGlu5 receptors or pharmacologic activation of mGlu2/3 or mGlu4/7/8 receptors produces neuroprotection in a variety of in vitro or in vivo models. MGlul receptor antagonists are promising drugs for the treatment of brain ischemia or for the prophylaxis of neuronal damage induced by synaptic hyperactivity. MGlu5 receptor antagonists may limit neuronal damage induced by a hyperactivity of N-methyl-d-aspartate (NMDA) receptors, because mGlu5 and NMDA receptors are physically and functionally connected in neuronal membranes. A series of observations suggest a potential application of mGlu5 receptor antagonists in chronic neurodegenerative disorders, such as amyotrophic lateral sclerosis and Alzheimer disease. MGlu2/3 receptor agonists inhibit glutamate release, but also promote the synthesis and release of neurotrophic factors in astrocytes. These drugs may therefore have a broad application as neuroprotective agents in a variety of CNS disorders. Finally, mGlu4/7/8 receptor agonists potently inhibit glutamate release and have a potential application in seizure disorders. The advantage of all these drugs with respect to NMDA or AMPA receptor agonists derives from the evidence that mGlu receptors do not "mediate," but rather "modulate" excitatory synaptic transmission. Therefore. it can be expected that mGlu receptor ligands are devoid of the undesirable

effects resulting from the inhibition of excitatory synaptic transmission, such as sedation or an impairment of learning and memory. Descriptors—Author Keywords: mGlu receptors; neuroprotection; subtype-selective ligands

Identifiers--KeyWord Plus(R): GROWTH-FACTOR-BETA; CEREBELLAR GRANULE CELLS; EXCITOTOXIC NEURONAL DEATH; RAT HIPPOCAMPAL SLICES; CULTURED CORTICAL-NEURONS; ISCHEMIC BRAIN INJURY; AMINO-ACID RECEPTORS; PROTEIN-KINASE-C; GROUP-III MGLUR; GROUP-I MGLURS